D. Gaylord
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PATENT
071949-1314

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Kenneth F. Buechler

Serial No.: 09/805,653

Title: DIAGNOSTIC DEVICES AND APPARATUS FOR THE CONTROLLED MOVEMENT OF REAGENTS WITHOUT MEMBRANES

Filing Date: March 13, 2001

Group Art Unit: 1743

Examiner: LYLE ALEXANDER

CERTIFICATE OF MAILING

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APPEAL BRIEF

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicant (herein, "Appellant") hereby appeals the Final Rejection of claims 74-100.

This Appeal Brief is accompanied by the requisite fee set forth in 37 C.F.R. § 1.17(f). If this fee is incorrect or if any additional fees are due in this regard, please charge or credit our Deposit Account No. 50-0872 for the appropriate amount.

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Real Party in Interest

The real party in interest in this appeal is Biosite, Inc. (formerly Biosite Diagnostics, Inc.), which is the assignee of the present application.

Related Appeals and Interferences

Appellant is not aware of any related appeals or interferences that may have a bearing on the board's decision in the pending appeal.

Status of Claims

On October 23, 2002, Appellant appealed from the Examiner's Action of June 24, 2002, making final the rejection of claims 74-100. These claims stand finally rejected under 35 U.S.C. §102 (b). Claims 1-73 were canceled without prejudice by Applicant during prosecution.

Status of Amendments

On September 24, 2002 Appellant submitted an amendment under 37 C.F.R. §1.116 to the Examiner's Action of June 24, 2002. As discussed hereinafter, the Examiner's rejection of the claims is based upon the incorrect assertion that the phrase "a plurality of target ligands" may be interpreted to mean "a plurality of molecules of the same molecular species." In order to assist the Examiner in correctly interpreting the phrase at issue, Applicant sought to amend the foregoing phrase to recite "a plurality of <u>different</u> target ligands." In an Advisory Action dated October 28, 2002, the Examiner indicated that the amendment submitted on September 24, 2002 would not be entered for the purposes of Appeal.

Appellant has also submitted an amendment concurrently with the present Appeal Brief in order to correct typographic errors in claims 89 and 95. No action has yet been taken with regard to the amendment submitted with the Appeal Brief.

Applicant provides the claims as currently pending in Appendix A of this Appeal Brief, the claims as amended by Appellant's submission of October 28, 2002 in Appendix B of this Appeal Brief, and the claims as amended by Appellant's submission concurrent with the Appeal Brief in Appendix C of this Appeal Brief.

Summary of The Invention

The invention relates generally to devices for conducting assays for determining the presence or amount of one or more analytes (referred to in the claims as "target ligands") in a single test format, and methods for use of such devices. *See, e.g.*, specification, page 1, lines 20-23. As presently claimed, the devices are constructed to determine the presence or amount of a plurality of target ligands at a single diagnostic element on a nonabsorbent surface within a capillary space. This diagnostic element comprises a plurality of discrete capture zones, each of which bind one of the plurality of target ligands of interest.

Numerous test systems for the detection of an analyte in fluid samples had been described prior to the present invention. In general, these devices included an absorbent paper or membrane to provide fluid flow, using the "wicking" properties of these absorbent materials to draw fluid to a set of test reagents that are designed to generate a visible signal that depends upon the presence or amount of the analyte of interest. *See, e.g.*, specification, page 1, line 26, through page 2, line 24 for a description of such devices. As noted in the instant specification, the use of such

absorbent, or "bibulous," materials can result in a lack of reproducibility in manufacture, as the characteristics of bibulous materials can be both variable and difficult to control. In addition, bibulous materials can be susceptible to non-specific binding of molecules other than the analyte of interest. *See, e.g.*, specification, page 5, lines 3-10.

Rather than using bibulous materials to provide fluid flow, alternative devices were designed that provide fluid movement rely by spacing walls at a distance that induces capillary force. An example of such devices is provided in U.S. Patent No. 4,948,961 ("the '961 patent"), which is relied upon by the Examiner in rejecting the instant claims. As noted, *e.g.*, in column 2, lines 45-51, of the '961 patent, the capillary space defined by the device walls acts "as a pump" to provide fluid flow to the set of test reagents that are designed to generate a visible signal. Even in these devices, absorbent material was often used to provide such reagents. '961 patent, column 16, lines 52-56. Moreover, for the detection of more than one analyte, the '961 patent indicates that an equivalent number of capillary chambers should be provided, "allowing for detection of a plurality of epitopic sites." '961 patent, description of Fig. 3 beginning in column 20, line 48.

The devices and methods of the present invention overcome the problems of devices that use absorbent materials for the immobilization of reagents or to control the flow of the reagents through the device, and circumvent the need to provide multiple capillary spaces for the detection of multiple analytes. In particular, the present invention provides a diagnostic element that comprises a capillary space through which a sample flows. Within this capillary space is a nonabsorbent surface that comprises a plurality of discrete capture zones, each of which bind for detection one of a plurality of target ligands of interest. *See, e.g.*, claim 74. In various alternative

embodiments, the discrete capture zones may comprise particles immobilized to the nonabsorbent surface, where the particles are adapted to capture the individual target ligands (*e.g.*, claim 79); or the assay device comprises an additional element that serves to control fluid flow through the device, referred to in the instant specification as a "time gate" (*e.g.*, claim 78).

Issues

Whether claims 74-100, which refer to assay devices comprising, *inter alia*, (i) a diagnostic element comprising a capillary space through which said sample flows, (ii) a non-absorbent surface within the capillary space, and (iii) a plurality of discrete capture zones on the nonabsorbent surface, each discrete capture zone comprising a capture element that binds one of the plurality of target ligands, and methods for using such devices, are anticipated under 35 U.S.C. §102 (b) by Hillman *et al.*, U.S. Patents 4,756,884 or 4,948,961.

Grouping of Claims

Claims 74-77 stand or fall together; each of claims 78-88 stand or fall alone; claims 89-92 and 94 stand or fall together; claim 93 stands or falls alone; claims 95-98 and 100 stand or fall together; and claim 99 stands or falls alone.

Specifically, claims 74-77 refer to assay devices for determining the presence or amount of a plurality of target ligands in a sample, the devices comprising (i) a diagnostic element comprising a capillary space through which said sample flows, (ii) a non-absorbent surface within the capillary space, and (iii) a plurality of discrete capture zones on the nonabsorbent surface, each discrete capture zone comprising a capture element that binds one of the plurality

of target ligands; claim 78 refers to such an assay device, further comprising a time gate; claim 79 refers to such an assay device, further comprising particles immobilized at the discrete capture zones; claims 80-88 each refer to such particles that have specific characteristics; claims 89-92 and 94 refers to methods for using the devices of claim 74; claim 93 refers to such methods, where the device further comprising particles immobilized at the discrete capture zones; claims 95-98 and 100 refer to methods in which the devices of claim 74 are used in a competitive assay; and claim 99 refers to such methods, where the device further comprising particles immobilized at the discrete capture zones.

Argument

Appellant respectfully submits that the Examiner's rejection under 35 U.S.C. § 102 over U.S. Patents 4,756,884 or 4,948,961 is based upon a flawed interpretation of the instantly claimed invention. The Examiner asserts that the phrase "a plurality of target ligands" is "only directed to a plurality of target ligands and not a plurality of different target ligands," and that, therefore, many identical molecules of the same analyte constitute a "plurality of target ligands," and many identical antibodies bound to a surface constitute "a plurality of discrete capture zones." Paper No. 11, pages 2-3. This flawed assertion fails to consider the claims as would one of ordinary skill in the art in light of the specification. Furthermore, with regard to the dependent claims, the Examiner has failed to address each and every element of the instant claims.

Therefore, because no *prima facie* case of anticipation has been established, Appellant respectfully requests that the rejection of claims 74-100 under 35 U.S.C. §102(b) be withdrawn or reversed, and that the instant claims be permitted to proceed to allowance.

Applicable Legal Standard

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the teaching of the specification, and with the understanding of the skilled artisan. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). *See also*, MPEP §2131. A patentee is free to be his or her own lexicographer and provide a particular meaning to a term or a phrase used in a claim, so long as that meaning is made clear in the specification or file history. *In re Weiss*, 26 USPQ2d 1885, 1887 (Fed. Cir. 1993); *See also*, MPEP § 2173.05(a).

The Examiner's prima facie case is fatally flawed due to a failure to properly consider the claimed invention

The Examiner's initial rejection of the instant claims stated only that "[t]he Hillman et al. references teach an assay device and a method of use. The device has a non-absorbent surface and capillary channels to draw the fluid sample through. The capillary channels contain the claimed beads functionalized by haptens, ligands, antibodies or enzymes which read on the claimed capture elements." Paper No. 7. The statement of rejection failed, however, to provide a *prima facie* case of anticipation by failing to indicate how the cited publications anticipate devices and methods in which a plurality of target analytes are immobilized at a plurality of discrete capture zones on a single diagnostic element surface. The Examiner also failed to indicate how the particles disclosed in the cited publications, which are never immobilized on a surface, anticipate those instant claims in which particles are immobilized at each discrete capture zone.

Appellant's response to this initial Office Action (mailed April 11, 2002) indicated these flaws in the Examiner's putative *prima facie* case of anticipation. Appellant noted that nothing in the cited publications "indicates that any one 'bead' contains a plurality of discrete capture zones for different analytes [and that] no other single non-absorbent surface contains a plurality of discrete capture zones, as the 'beads' disclosed by the Hillman patents are 'included in the medium' ('961 patent, column 10, lines 20-58) so that they may be crosslinked for detection; thus, these beads are not immobilized on a surface as discrete capture zones." Response to Office Action mailed April 11, 2002, page 3.

In response, the Examiner offered the unsubstantiated opinion that the phrase "a plurality of target ligands" is "only directed to a plurality of target ligands and not a plurality of <u>different</u> target ligands," and that, therefore, a plurality of molecules of the same analyte on a single bead constitutes a plurality of target ligands, and a plurality of individual antibodies bound to a surface constitute a plurality of discrete capture zones. Paper No. 11, pages 2-3. The Examiner does not provide any evidence or reasoning as to why the skilled artisan would apply this meaning to the phrase "a plurality of target ligands." Instead, the Examiner merely asserted that it is so.

The skilled artisan would readily acknowledge that the phrase "plurality of target ligands" refers to two or more different molecular species that are detected in an assay

Appellant respectfully submits that the Examiner's rejection is based upon a flawed interpretation of the instantly claimed invention. While the Examiner is entitled to give claims their broadest reasonable interpretation, "this interpretation must be consistent with the one that those of skill in the art would reach." *In re Cortright*, 49 USPQ2d 1464, 1467 (Fed. Cir. 1999).

The Examiner' position that the phrase "a plurality of target ligands" does not refer to different ligands, and that this phrase might refer to a number of molecules of the same ligand is contrary to the teachings of the instant specification and the understanding of those of skill in the art.

The skilled artisan would understand that a "target ligand" is an analyte - one particular molecular species, which may exist as many molecules of the same species - that is the subject of detection in an assay. The skilled artisan would also readily acknowledge that a reference to assays measuring more than one target ligand does not refer to discrimination amongst individual identical molecules, but rather the detection of different molecular species. Thus, a "plurality of target ligands" as recited in the instant claims refers to two or more different molecular species that are detected in an assay, and not two or more molecules of a single species of target ligand.

For example, the assay devices of the present invention are described in the instant specification on page 5, lines 30-32 (emphasis added):

> The assay devices, assay systems and device component of this invention can comprise two opposing surfaces disposed a capillary distance apart; at least one of the surfaces comprises the ability to detect at least one target ligand or a conjugate in an amount related to the presence or amount of target ligand in a sample.

Likewise, the diagnostic element recited in the instant claims is described on page 25, lines 3-16, as comprising:

> reagents, such as receptors, or devices, such as biosensors which bind or react with one or more components from the reaction mixture.... One or more receptors or biosensors can be placed on the diagnostic element to measure the presence or amount of one or more target ligands. The receptors or biosensors can be placed

> in discrete zones... [or a] single receptor or biosensor can be placed over the majority of the diagnostic element.

From these passages, the skilled artisan would understand that "a single target ligand" refers, not to a single molecule, but rather to a single molecular species of target ligand which may be composed of many identical molecules. Any other interpretation is inconsistent with detecting the "presence or amount" of a target ligand, as the skilled artisan would understand that one could only detect the presence of a single molecule, and not the "amount" of a single molecule. Because the Examiner's interpretation of the claims renders meaningless the phrase "detecting the amount" in the specification and claims, the Examiner's interpretation cannot be correct.

Similarly, the skilled artisan would clearly understand that "a single receptor" for a single target ligand refers, not to a single molecule, but rather to a single molecular species of receptor which may be composed of many molecules. Any other interpretation is inconsistent with the statement in the specification that a single receptor may be distributed over the entire diagnostic element, as a single molecule could not be distributed in this manner.

Consistent with the foregoing, the skilled artisan would understand that the phrase "a plurality of target ligands" refers to a plurality of different molecular species, and cannot mean a plurality of identical molecules, each of which is separately detected. Unlike the Examiner's flawed interpretation, this interpretation of the phrase relies on the information in the specification to properly interpret the phrase. The Examiner's failure to properly consider the

specification "improperly expand[s] the meaning of a claim term beyond that intended by the inventor as described in the disclosure." *In re Weiss*, 26 USPQ2d 1885, 1887 (Fed. Cir. 1993).

Moreover, the foregoing interpretation of the phrase "a plurality of target ligands" is fully consistent with the meaning that is ascribed to like terms by those of skill in the art, such as that seen in the Hillman patents cited in by the Examiner in the very rejection at issue, while the Examiner's interpretation of the phrase is inconsistent with such a meaning. For example, in column 20, lines 48-50, the '961 patent refers to "a device which is exemplary of the determination of a plurality of analytes in a single sample." This section of the '961 patent describes the "plurality of analytes" as different antigens "indicative of the particular serotype" of pathogen in a sample, and not as not a plurality of identical molecules, each of which is separately detected. '961 patent, column 21, lines 7-14. Appellant respectfully submits that such usage in "[p]rior art references [is] indicative of what all those skilled in the art generally believe a certain term means." *In re Cortright*, 49 USPQ2d 1464, 1467 (1999).

Appellant has clearly defined the phrase "plurality of target ligands" as referring to "different analytes" in the specification, as well as in the file history

Furthermore, even if it is true that the phrase "plurality of target ligands" may naively be interpreted in the manner to which the Examiner refers, Appellant respectfully submits that a patentee is free to be his or her own lexicographer in providing a meaning to a phrase, so long as that meaning is made clear in the specification or file history. *See*, e.g., MPEP § 2173.05(a); *see also*, *In re Weiss*, 26 USPQ2d 1885, 1887 (Fed. Cir. 1993) ("When the applicant states the meaning that the claim terms are intended to have, the claims are examined with that meaning, in

order to achieve a complete exploration of the applicant's invention and its relation to the prior art"). The understanding that the skilled artisan would take from the specification is discussed above. Appellant further respectfully submits that, in the file history, Appellant has made clear that, for purposes of the present application, the phrase "a plurality of target ligands" refers to different ligands. The Examiner has simply ignored Appellants clear statements in this regard.

When the claims are properly considered, the cited publications fail to teach each and every limitation of the instant claims

When the instant claims are properly interpreted, it is clear that the cited Hillman patents do not disclose a single non-absorbent surface within a capillary space comprising a plurality of discrete (*i.e.*, discontinuous) capture zones corresponding to a plurality of analytes, as recited in the present claims. The Examiner contends that columns 20 and 21 of the cited publications "use a variety of reagents for the detection of a variety of different analytes." Paper No. 11, page 3. Whether or not this is true, however, is irrelevant to the instant claims. The Examiner has failed to address each and every element of the instant claims, which refer to a diagnostic element comprising a capillary space; a non-absorbent surface in that capillary space; and a plurality of discrete capture zones on that non-absorbent surface corresponding to the plurality of target ligands. Thus, no *prima facie* case of anticipation has been established. *See*, MPEP § 2131 (in order to anticipate a claim, the identical invention must be shown in as complete detail as is contained in the claim).

Appellant also respectfully submits that, in those embodiments in which the cited publications disclose detection of more than one analyte, the cited publications disclose

separating the flow into multiple capillary spaces, none of which detects more than a single analyte. *See, e.g.*, description of figure 4 in the '961 patent, column 21, lines 37-68:

> Chamber 128 is divided into two half chambers or semichambers 136 and 138. In semichamber 136, two reagents are present indicated by the slanted lines and the crosses. The slanted lines are monoclonal antibodies specific for an epitope on the analyte, where the antibodies are non-diffusively bound on the surface. The crosses indicate monoclonal antibodies conjugated to fluorescers, where the monoclonal antibodies bind to a different epitope of the analyte. The fluorescer conjugate is reversibly bound to the surface of the two chambers 136 and 138 in the area near the entry ports 140 and 142 of capillary 126....

Thus, the cited publications do not disclose any assay devices comprising a plurality of discrete capture zones on a single non-absorbent surface in a capillary space for determining the presence or amount of a plurality of target ligands in a sample, as required by the instant claims.

Furthermore, the present claims refer to "a non-absorbent surface comprising a plurality of discrete capture zones." Nothing in the cited publications indicates that any one reagent contains a plurality of discrete (*i.e.*, discontinuous) capture zones for different analytes. In particular, the "reagent" disclosed by the cited publications do not comprise discrete capture zones on their own surfaces; nor are they immobilized on a single nonabsorbent surface to provide discrete capture zones. *See, e.g.*, description of figure 3 in the '961 patent, column 20, line 47, through column 21, line 24 (For the detection of multiple analytes, reagents in chamber 108 bind to a common epitope. In each of three separate chambers 96, 98, and 100, reagents corresponding to individual serotype antigens are used to agglutinate the reagents originating in (and flowing from) chamber 108 if that serotype is present in the original sample. Detection of another (undisclosed) analyte in the sample may take place in yet another chamber 106). Thus,

the cited publications make it clear that any detection of multiple analytes must occur in separate spaces, and not in a common capillary space comprising a plurality of discrete capture zones on a surface.

Therefore, because the cited publications do not teach and suggest every limitation of the claimed invention, no *prima facie* case of anticipation has been established. Accordingly, Appellant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn or reversed.

Conclusion

For the reasons discussed above, the instant claims are in condition for allowance, and Appellants respectfully request that the claims be allowed to issue.

Respectfully submitted,

Dated: January 7, 2003

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Appendix A: Text of the Claims Involved in the Appeal

74. An assay device for determining the presence or amount of a plurality of target ligands in a sample, the device comprising:

a diagnostic element comprising a capillary space through which said sample flows, comprising (i) a non-absorbent surface within said capillary space, and (ii) a plurality of discrete capture zones on said nonabsorbent surface, each discrete capture zone comprising a capture element that binds one target ligand in said plurality of target ligands.

75. The assay device of claim 74, comprising at least 50 said discrete capture zones, corresponding to at least 50 target ligands.

76. The assay device of claim 74, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

77. The assay device of claim 74, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

78. The assay device of claim 74, wherein said device further comprises a chamber fluidly connected to said diagnostic element, and a time gate that delays fluid flow between said chamber and said diagnostic element.

79. The assay device of claim 74, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

80. The device of claim 79 wherein the particles are latex.

81. The device of claim 79 wherein the particles are polystyrene.

82. The device of claim 79 wherein the particles are nanoparticles.

83. The device of claim 82 wherein the nanoparticles comprise silica, zirconia, alumina, titania, ceria, metal sols, or polystyrene.

84. The device of claim 82 wherein the nanoparticles have sizes in a range from about 1 nm to 100 nm.

85. The device of claim 82 wherein the nanoparticles are immobilized on said nonabsorbent surface through adsorption or covalent bonds.

86. The device of claim 79 wherein said particles are immobilized on said nonabsorbent surface by magnetic means, hydrophobic means, hydrogen bonding, electrostatic means, or entrapment.

87. The device of claim 79, wherein said particles have diameters ranging from about 0.1 mm to 10 mm.

88. The device of claim 79, wherein said receptor is immobilized on a surface of the particle.

89. A method for determining the presence or amount of a plurality of target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a labeled reagent that binds to said plurality of target ligands,

whereby said sample and said labeled reagent flow through said capillary space for capture of each said target ligand at its corresponding capture zone; and

generating a plurality of detectable signals from label bound to each target ligand at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of target ligands in said sample.

90. The method of claim 89, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 target ligands.

91. The method of claim 89, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

92. The method of claim 89, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

93. The method of claim 89, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

94. The method of claim 89, wherein said labeled reagent is a fluorescently labeled reagent.

95. A method for determining the presence or amount of a plurality of target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a plurality of ligand analogue conjugates, each ligand analogue conjugate corresponding to one of said plurality of target ligands,

whereby said sample and said plurality of ligand analogue conjugates flow through said capillary space, whereby each target ligand competes with its corresponding ligand analogue conjugate for capture at its corresponding capture zone; and

generating a plurality of detectable signals from ligand analogue conjugate bound at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of target ligands in said sample.

96. The method of claim 95, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 target ligands.

97. The method of claim 95, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

98. The method of claim 95, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

99. The method of claim 95, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

100. The method of claim 95, wherein said ligand analogue conjugate is a fluorescently labeled ligand analogue conjugate.

Appendix B: Text of the Claims Amended in Appellant's Submission of September 24, 2002

74. (Amended) An assay device for determining the presence or amount of a plurality of different target ligands in a sample, the device comprising:

a diagnostic element comprising a capillary space through which said sample flows, comprising (i) a non-absorbent surface within said capillary space, and (ii) a plurality of discrete capture zones on said nonabsorbent surface, each discrete capture zone comprising a capture element that binds one target ligand in said plurality of different target ligands.

75. (Amended) The assay device of claim 74, comprising at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

89. (Amended) A method for determining the presence or amount of a plurality of different target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a labeled reagent that binds to said plurality of target ligands,

whereby said sample and said labeled reagent flow through said capillary space for capture of each said different target ligand at its corresponding capture zone; and

generating a plurality of detectable signals from label bound to each different target ligand at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of different target ligands in said sample.

90. (Amended) The method of claim 89, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

95. (Amended) A method for determining the presence or amount of a plurality of different target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a plurality of ligand analogue conjugates, each ligand analogue conjugate corresponding to one of said plurality of different target ligands,

whereby said sample and said plurality of ligand analogue conjugates flow through said capillary space, whereby each different target ligand competes with its corresponding ligand analogue conjugate for capture at its corresponding capture zone; and

generating a plurality of detectable signals from ligand analogue conjugate bound at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of different target ligands in said sample.

96. (Amended) The method of claim 95, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

Appendix C: Text of the Claims Amended in an Amendment Submitted Concurrently with this Appeal Brief

89. (Amended) A method for determining the presence or amount of a plurality of target ligands in a sample, the method comprising:

contacting the diagnostic element of claim [1] 74 with

(i) a sample, and

(ii) a labeled reagent that binds to said plurality of target ligands,

whereby said sample and said labeled reagent flow through said capillary space for capture of each said target ligand at its corresponding capture zone; and

generating a plurality of detectable signals from label bound to each target ligand at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of target ligands in said sample.

95. (Amended) A method for determining the presence or amount of a plurality of target ligands in a sample, the method comprising:

contacting the diagnostic element of claim [1] 74 with

(i) a sample, and

(ii) a plurality of ligand analogue conjugates, each ligand analogue conjugate corresponding to one of said plurality of target ligands,

whereby said sample and said plurality of ligand analogue conjugates flow through said capillary space, whereby each target ligand competes with its corresponding ligand analogue conjugate for capture at its corresponding capture zone; and

generating a plurality of detectable signals from ligand analogue conjugate bound at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of target ligands in said sample.